Letter

The role of poly (ADP-ribose) polymerase in ventilator-induced lung injury

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See related research by Kim *et al.*, http://ccforum.com/content/12/4/R108

With interest we have read the paper by Kim and colleagues reporting the role of poly (ADP-ribose) polymerase (PARP) in ventilator-induced lung injury (VILI) in healthy mice [1].

Some issues have not been addressed appropriately. The authors show increased levels of TNFα in lung homogenate after 2 hours of lung-protective ventilation (LPV). Previous data from our laboratory have shown in the healthy mouse lung that so-called protective mechanical ventilation (tidal volume, 8 ml/kg; peak airway pressure, 10 to 12 cmH_2O; positive end-expiratory pressure, 4 cmH_2O) induces a pulmonary inflammatory response [2]. In addition to elevated levels of TNFα, we found increased expression of IL-1β, IL-6, and keratinocyte-derived chemokine in the lung homogenate and found an increased number of pulmonary leucocytes in mice mechanically ventilated for 2 hours. Electron microscopy revealed evidence for type I pneumocyte membrane disruption and endothelial detachment, indicating structural injury. In line with the findings by Kim and colleagues, the wet/dry ratio was not affected after 2 hours of mechanical ventilation – although in our study 4 hours of protective ventilation did increase the wet/dry ratio.

The so-called LPV-induced pulmonary inflammation can therefore occur without activation of PARP. It is possible that initiation of inflammation precedes the activation of PARP. Do the authors have any information on the time dependency of PARP activation in relation to the activation of proinflammatory cytokines? In addition, it would be of interest to identify the type of cells exhibiting elevated PARP activity – for instance, perhaps by double staining with leukocyte markers. In our opinion, the clinical relevance of the study is limited due to very high peak airway pressures used.

Authors' response

Je Hyeong Kim and Kyung Ho Kang

The main background for our study is that LPV cannot completely eliminate the consequences of VILI, inducing lung inflammation with changes in the parameters of VILI [1]. Vaneker and colleagues indicate that the changes of biologic markers in bronchoalveolar lavage fluid, not in lung homogenate, and the changes of the wet-to-dry weight ratio in the LPV group were different from those in their study [2]. Reviewing the experimental studies about VILI, changes in the biological markers and the parameters of VILI, even in LPV settings, could differ depending on the experimental conditions – including the animals used, the conditions of mechanical ventilation, the specimens, and the analysis methods. The degree and time-course of the changes in parameters might therefore be different in each experiment and may show discrepancies among studies, especially in LPV settings in which inflammatory insults are more subtle than the VILI settings [3,4].

Although overactivation of PARP has been reported as one of pivotal mechanisms of inflammation, it cannot explain the entire complicated process of inflammation. Subtle inflammation of the LPV group in our study might therefore be induced by other pathways or by low-grade PARP activation under the detection level of the analysis method used. In contrast to the

IL = interleukin; LPV = lung-protective ventilation; PARP = poly (ADP-ribose) polymerase; TNF = tumour necrosis factor; VILI = ventilator-induced lung injury.

diseased lungs, normal lungs are relatively insusceptible to the detrimental effects of mechanical ventilation [3]. To investigate newer pathogenetic mechanisms of VILI with a normal lung model, a higher pressure or tidal volume, which might not be clinically relevant, is frequently necessary to induce appropriate lung injury.

Competing interests

The authors declare that they have no competing interests.

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